**Amendments to the Specification:**

Please replace the paragraph beginning at page 1, line 9, with the following rewritten paragraph:

Cross-Reference to Related Application

--This application is a divisional of the U.S. Patent Application Serial No. 08/931,645, filed September 16, 1997, now U.S. Patent No. 6,096,551, which application is a divisional of U.S. Patent Application Serial No. 08/300,386, filed September 2, 1994, now U.S. Patent No. 5,667,988, which application is a continuation-in-part of U.S. Patent Application 08/174,674, filed December 28, 1993, now abandoned, which application is a continuation of U.S. Patent Application Serial No. 07/826,623, filed January 27, 1992, now abandoned.--

Please replace the paragraph beginning at page 42, line 9, with the following rewritten paragraph:

--The vector also contained a ribosome binding site as described by Shine et al., Nature, 254:34 (1975). The sequence of the phagemid vector, ~~pBluescript~~ PBLUESCRIPT , which includes ColE1 and F1 origins and a beta-lactamase gene, has been previously described by Short et al., Nuc. Acids Res., 16:7583-7600 (1988) and has the GenBank Accession Number 52330 for the complete sequence. Additional restriction sites, Sal I, Acc I, Hinc II, Cla I, Hind III, Eco RV, Pst I and Sma I, located between the Xho I and Spe I sites of the empty vector were derived from a 51 base pair stuffer fragment of ~~Pbluescript~~ PBLUESCRIPT as described by Short et al., supra. A nucleotide sequence that encodes a flexible 5 amino acid residue tether sequence which lacks an ordered secondary structure was

juxtaposed between the Fab and cp3 nucleotide domains so that interaction in the expressed fusion protein was minimized.--

Please replace the paragraph beginning at page 46, line 8, with the following rewritten paragraph:

--For overlap PCR, each set of PCR reactions were performed in a 100 microliter (ul) reaction containing 1 microgram (ug) of each of oligonucleotide primers listed above in a particular pairing, 8 ul 2.5 Mm dNTP's (DATP, DCTP, DGTP, DTTP), 1 ul ~~Taq~~ TAQ polymerase, 10 ng of template pC3AP313, and 10 ul of 10X PCR buffer purchased commercially (Promega Biotech, Madison, WI). Thirty-five rounds of PCR amplification in a Perkin-Elmer Cetus 9600 ~~GeneAmp~~ GENEAMP PCR System thermocycler were then performed. The amplification cycle consisted of denaturing at 94 degrees C (94C) for 1 minute, annealing at 47C for 1 minute, followed by extension at 72C for 2 minutes. To obtain sufficient quantities of amplification product, 15 identical PCR reactions were performed.--

Please replace the paragraph beginning at page 48, line 15, with the following rewritten paragraph:

--One hundred nanograms of gel purified products from the first and second PCR reactions were then admixed with 1 ug each of KEF and T7B oligonucleotide primers as a primer pair in a final PCR reaction to form a complete light chain fragment by overlap extension. The PCR reaction admixture also contained 10 ul of 10X PCR buffer, 1 ul ~~Taq~~ TAQ polymerase and 8 ul 2.5 Mm DNTP'S as described above.--

Please replace the paragraph beginning at page 57, line 35, with the following rewritten paragraph:

--One hundred nanograms of gel purified products from the first and second PCR reactions were then admixed with 1 ug each of FTX3 and R3B oligonucleotide primers as a primer pair in a final PCR reaction to form a complete heavy chain fragment by overlap extension. The PCR reaction admixture also contained 10 ul 10X PCR buffer, 1 ul ~~Taq~~ TAQ polymerase and 8 ul 2.5 Mm DNTP'S as described above. The PCR reaction was performed as previously described.--

Please replace the paragraph beginning at page 70, line 4, with the following rewritten paragraph:

--The phage libraries produced in Example 4A, 4B and 4C were panned as described herein on ~~microtiter~~ MICROTITER plates coated with the synthetic hapten conjugate target molecules. Three synthetic haptens were chosen for screening for improved high affinity antibodies having either a randomized heavy or light chain domain or both. The conjugates, shown in Figure 1 and labeled as 1, 2, and 3, respectively, were fluorescein-BSA (Fl-BSA), S-BSA, an analog for the selection of catalytic antibodies that catalyze a decarboxylation reaction, and C-BSA, similar to the other two haptens but containing a flat aromatic ring system and lacking the anionic character of the other haptens. Conjugate 1 was described by Barbas et al., Proc. Natl. Acad. Sci., USA, 89:4457-4461 (1992), the disclosure of which is hereby incorporated by reference. Conjugates 2 and 3 have been previously described by Lewis et al., Reports, 1019-1021 (1991), the disclosure of which is hereby incorporated by reference. The reagents were used at a concentration of 40 ug/ml in the coating buffer, 0.1 M bicarbonate at Ph 8.6.--

Please replace the paragraph beginning at page 70, line 26, with the following rewritten paragraph:

--The panning procedure described was a modification of that originally described by Parmley et al., Gene, 73:305-318 (1988). This procedure, described below for one preparation, was followed for each of the phage preparations for all libraries prepared for use in this invention. Since the haptens were conjugated to BSA, selective pressure was applied to select for hapten binding and against BSA binding. This was accomplished by resuspending phage in TBS containing 1% BSA prior to selection and by alternating 3% BSA and 2% non-fat dry milk blocking of the ~~microtiter~~ MICROTITER dish at each round of selection.--

Please replace the paragraph beginning at page 71, line 3, with the following rewritten paragraph:

--Wells of a ~~microtiter~~ MICROTITER plate (Costar 3690) were separately coated overnight at 4C with the purified target conjugates prepared above. The wells were washed twice with water and blocked by completely filling the well with 3% (w/v) bovine serum albumin (BSA) in PBS and incubating the plate at 37C for 1 hour. Blocking solution was removed by shaking, 50 ul of each of the phage libraries prepared above (typically $10^{11}$ cfu) were added to each well, and the plate was incubated for 2 hours at 37C.--

Please replace the paragraph beginning at page 74, line 8, with the following rewritten paragraph:

--Preliminary ELISA assays were performed to first characterize the binding specificity of the panned phage

semisynthetic Fab antibodies prepared above toward synthetic haptens. For ELISA, 1 ug/well of the synthetic haptens prepared in Example 5B was separately admixed to individual wells of a ~~microtiter~~ MICROTITER plate and maintained at 4C overnight to allow the hapten solution to adhere to the walls of the well. After the maintenance period, the wells were washed once with PBS and thereafter maintained with a solution of 3% BSA to block nonspecific sites on the wells. The plates were maintained at 37C for 1 hour after which time the plates were inverted and shaken to remove the BSA solution. Soluble Fab heterodimers expressing the semisynthetic Fab heterodimers prepared in Example 5C were then admixed separately to each well and maintained at 37C for 1 hour to form a immunoreaction products. Following the maintenance period, the wells were washed 10 times with PBS to remove unbound soluble antibody and then maintained with a secondary goat anti-human FAB conjugated to alkaline phosphatase diluted in PBS containing 1% BSA. The wells were maintained at 37C for 1 hour after which the wells were washed 10 times with PBS followed by development with p-nitrophenyl phosphate.--

Please replace the paragraph beginning at page 75, line 23, with the following rewritten paragraph:

--The affinities of several purified clones were examined by surface plasmon resonance. Only observed monomeric Fab as judged by gel filtration has been observed in contrast to a recent report of single-chain antibody dimerization as described by Griffiths et al., EMBO J., 12:725-734 (1993). The determination of on and off affinity constants, respectively, $k_{on}$ and $k_{off}$, for selected clones were performed using the ~~Biacore~~ BIACORE instrument from Pharmacia Biosensor (Piscataway, NJ, according to manufacturer's instructions. The Fl-BSA conjugate was immobilized in 10 Mm acetate buffer at Ph 2.5 to yield 600

resonance units on a CM5 ~~Biacore~~ BIACORE sensor chip. The $k_{on}$ and $k_{off}$ were determined by standard analysis in PBS at flow rates of 5 and 8 ul/minutes, respectively as described by Altschun et al., Biochem., 31:6298-6304 (1992).--

Please replace the paragraph beginning at page 76, line 24, with the following rewritten paragraph:

--Nucleic acid sequencing was performed on double-stranded DNA using ~~Sequenase~~ SEQUENASE 1.0 (USB, Cleveland, OH) encoding the specific soluble synthetic hapten-binding Fab heterodimers of this invention characterized above.--

Please replace the paragraph beginning at page 81, line 28, with the following rewritten paragraph:

--Following the excision of the lambda phage library encoding the light chain, eleven clones were randomly chosen for further analysis. DNA was isolated and the nucleotide sequence determined by the dideoxy chain-termination method (Sanger et al., Proc. Natl. Acad. Sci. U.S.A., 74:5463-5467 (1977)) using ~~Sequenase~~ SEQUENASE 2.0 (United States Biochem).--

Please replace the paragraph beginning at page 83, line 4, with the following rewritten paragraph:

--The phage library prepared in Example 8A was panned as described in Example 5B1 on ~~microtiter~~ MICROTITER plates coated with TPO target molecules to isolate phagemid displaying anti-TPO Fab heterodimers. Consecutive rounds of panning on TPO-coated ELISA plates resulted in an enrichment of approximately $10^4$-fold. Round 1 of panning gave a recovery of $2 \times 10^3$ colony forming units (cfu); round 2 gave a recovery of $3.2 \times 10^3$ cfu; round 3

gave a recovery of $>10^6$ cfu; and round 4 gave a recovery of $>10^7$ cfu. The panned phage surface expression clones were then converted into clones expressing soluble Fab antibodies as described in Example 5C for further characterization.--

Please replace the paragraph beginning at page 84, line 27, with the following rewritten paragraph:

--The nucleotide sequence of the specific soluble TPO-binding Fab heterodimers of this invention was determined. The nucleotide sequence of the anti-TPO monoclonal antibody 2G4 (Horimoto et al., Autoimmunity, 14:1-7 (1992) and Hexham, et al., Autoimmunity, 14:169-172 (1992)) and the SP series of recombinant anti-TPO antibodies (Portolano et al., Biochem. Biophys. Res. Comm., 179:372-377 (1991), Portolano et al., J. Clin. Invest., 90:720-726 (1992), and Portolano et al., J. Immunol., 150:880-887 (1993)) was also determined. Nucleic acid sequencing was performed on double-stranded DNA using ~~Sequenase~~ SEQUENASE 2.0 (USB, Cleveland, OH). The primers SEQGb, SEQKb, and the M13 reverse primer were used as described in Hexham et al., Autoimmunity, 12:135-141 (1992).--